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The Reactions of Esters of Amidosulfurous Acid

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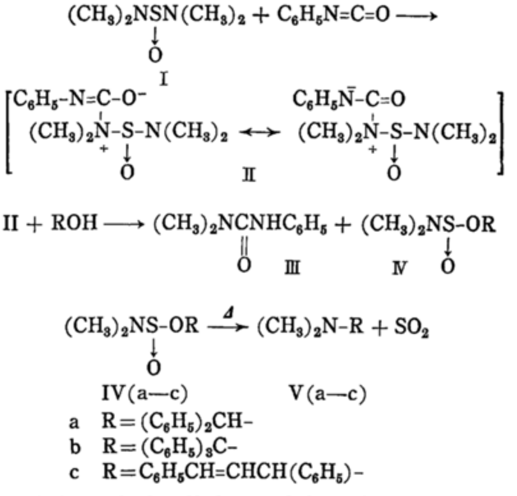
It was found that benzhydryl dimethylamidosulfite, obtained from *N,N,N′,N′*-tetramethylsulfurous diamide-phenyl isocyanate adduct and benzhydrol, decomposed to give benzhydryldimethylamine and sulfur dioxide. Similarly, triphenylmethyl and 1,3-diphenylallyl dimethylamidosulfite gave corresponding tertiary amines when these esters were refluxed in benzene. On the other hand, benzoin dimethylamidosulfite gave benzil, the oxidized product of benzoin. When β-anilinoethyl and β-*N*-methylaminoethyl dimethylamidosulfite were heated at 120—130°C for 10 min, cyclic esters of amidosulfurous acid, 3-phenyl- and 3-methyl-1,2,3-oxathiazolidine-2-oxide, were obtained along with evolution of dimethylamine. Further, the thermal decomposition of the cyclic compounds was studied.

In the preceding paper, it has been shown that tetraalkylsulfurous diamides (I) and phenyl isocyanate gave 1 : 1 adducts (II), which react readily with active hydrogen compounds such as alcohols, carboxylic acids and mercaptans to give *N,N*-dialkyl-*N′*-phenylureas (III), and alkyl dialkylamidosulfites, *N,N*-dialkylcarboxylic amides and *S*-alkyl dialkylamidothiosulfites, respectively.[1] This reaction is considered to be a convenient route for the synthesis of amidosulfurous acid derivatives, since I and phenyl isocyanate are readily available and the products are obtained in excellent yields under mild conditions by simple procedure.

As part of the investigation of the reactions of amidosulfurous acid derivatives,[1,2] the reactions of II with various alcohols such as α-substituted benzyl alcohols, α-ketoalcohols and aminoalcohols were studied in order to prepare the corresponding esters and to know the nature of the esters. When benzhydrol was added to a solution of II in dry ether, *N,N*-dimethyl-*N′*-phenylurea (III) was separated quantitatively and, after removal of the solvent, a viscous oily substance remained. The structure of this oily substance was assigned to be benzhydryl dimethylamidosulfite (IVa) by its infrared spectrum which has characteristic bands attributable to ester of amidosulfrous acid (1150 and 900 cm^{-1}). However, an attempt to purify this oily substance by vaccum distillation resulted in decomposition with evolution of sulfur dioxide. From the residue, benzhydryldimethylamine (Va) was isolated in a 50% yield. Similar decomposition was observed when triphenylmethyl and 1,3-diphenylallyl dimethylamidosulfites (IVb and IVc), obtained as viscous oily substance by the above mentioned procedure, were refluxed in dry benzene, and corresponding tertiary amines (Vb and Vc) were obtained in 50% and 59% yields, respectively.



$$(CH_3)_2N\underset{\overset{\downarrow}{O}}{S}N(CH_3)_2 + C_6H_5N{=}C{=}O \longrightarrow$$

I

$$\left[\begin{array}{c} C_6H_5\text{-}N{=}\overset{|}{C}\text{-}O^- \\ (CH_3)_2\underset{+}{N}\text{-}\underset{\overset{\downarrow}{O}}{S}\text{-}N(CH_3)_2 \end{array} \longleftrightarrow \begin{array}{c} C_6H_5\bar{N}\text{-}\overset{|}{C}{=}O \\ (CH_3)_2\underset{+}{N}\text{-}\underset{\overset{\downarrow}{O}}{S}\text{-}N(CH_3)_2 \end{array}\right]$$

II

$$\text{II} + ROH \longrightarrow (CH_3)_2N\underset{\overset{\|}{O}}{C}NHC_6H_5 + (CH_3)_2N\underset{\overset{\downarrow}{O}}{S}\text{-}OR$$

III IV

$$(CH_3)_2N\underset{\overset{\downarrow}{O}}{S}\text{-}OR \xrightarrow{\Delta} (CH_3)_2N\text{-}R + SO_2$$

IV(a—c) V(a—c)

a $R=(C_6H_5)_2CH$-
b $R=(C_6H_5)_3C$-
c $R=C_6H_5CH{=}CHCH(C_6H_5)$-

While, ethyl, allyl, cyclohexyl and benzyl dimethylamidosulfites are fairly stable and are able to be distilled under reduced pressure without decomposition.[1] Concerning the above results, Zinner[3] has reported that attempts to

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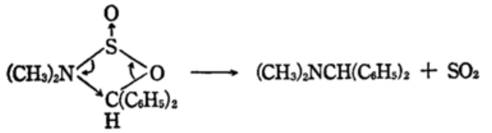
[1] T. Mukaiyama, H. Shimizu and H. Takei, *J. Org. Chem.*, **32**, 3475 (1967).

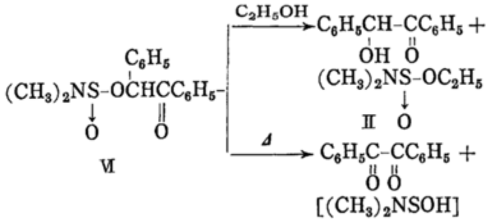
[2] T. Mukaiyama, H. Shimizu and H. Takei, This Bulletin, 40, 939 (1967).

[3] G. Zinner, *Angew. Chem.*, **69**, 93 (1959).

distill ethyl dialkylamidosulfites at atmospheric pressure resulted in decomposition with evolution of sulfur dioxide, but the corresponding tertiary amines could not be isolated. It can be noted that electron-withdrawing substituents, *e. g.* two phenyl groups, on α-carbon atom of the esters favor the reaction to afford tertiary amines probably proceeding through an internal nucleophilic attack by the amino group on α-carbon atom (SN*i* Mechanism).



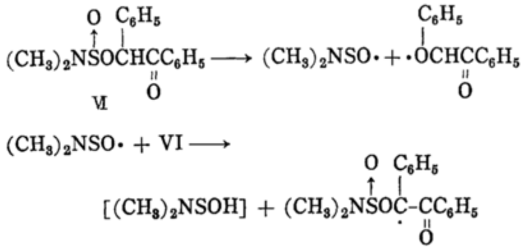
Next, it was established that the reaction of II with benzoin afforded benzoin dimethylamidosulfite (VI) as a viscous oily substance along with III. The structure of VI was confirmed by its infrared spectrum and the fact that treatment of VI with ethanol gave benzoin and ethyl dimethylamidosulfite (VII), transesterification products, in good yields. When VI was refluxed in dry benzene for an hour, the expected products, dimethylaminodeoxybenzoin and sulfur dioxide, could not be detected, instead, benzil, the oxidized product of benzoin, was obtained in a 74 % yield.



$$(CH_3)_2N\underset{O}{\underset{\downarrow}{S}}-O\overset{C_6H_5}{\overset{|}{C}}H\underset{O}{\underset{\parallel}{C}}C_6H_5 \xrightarrow{C_2H_5OH} C_6H_5\underset{OH}{\underset{|}{C}}H-\underset{O}{\underset{\parallel}{C}}C_6H_5 + (CH_3)_2N\underset{O}{\underset{\downarrow}{S}}-OC_2H_5$$

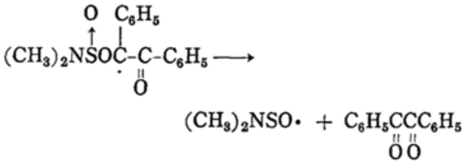
$$\xrightarrow{\Delta} C_6H_5\underset{O}{\underset{\parallel}{C}}-\underset{O}{\underset{\parallel}{C}}C_6H_5 + [(CH_3)_2NSOH]$$

It seemed reasonable to assume that benzil may be produced through radical intermediates based on the following results: When VI was heated in benzene in the presence of diphenylpicrylhydrazyl, violet color of the radical disappeared soon. In addition, it was found that addition of diethylaniline, which is known to be a radical scavenger, inhibit the decomposition of VI. Based on these results, the oxidation reaction can be explained by assuming the following radical chain mechanism.



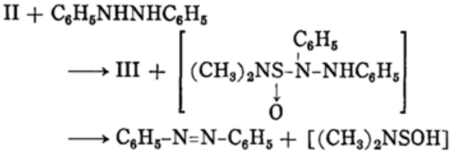
$$(CH_3)_2N\overset{O}{\overset{\uparrow}{S}}O\overset{C_6H_5}{\overset{|}{C}}H\underset{O}{\underset{\parallel}{C}}C_6H_5 \longrightarrow (CH_3)_2NSO\cdot + \cdot O\overset{C_6H_5}{\overset{|}{C}}H\underset{O}{\underset{\parallel}{C}}C_6H_5$$

$$(CH_3)_2NSO\cdot + VI \longrightarrow [(CH_3)_2NSOH] + (CH_3)_2N\overset{O}{\overset{\uparrow}{S}}O\overset{C_6H_5}{\overset{|}{\dot{C}}}-\underset{O}{\underset{\parallel}{C}}C_6H_5$$



$$(CH_3)_2N\overset{O}{\overset{\uparrow}{S}}O\overset{C_6H_5}{\overset{|}{\dot{C}}}-\underset{O}{\underset{\parallel}{C}}-C_6H_5 \longrightarrow (CH_3)_2NSO\cdot + C_6H_5\underset{O}{\underset{\parallel}{C}}\underset{O}{\underset{\parallel}{C}}C_6H_5$$

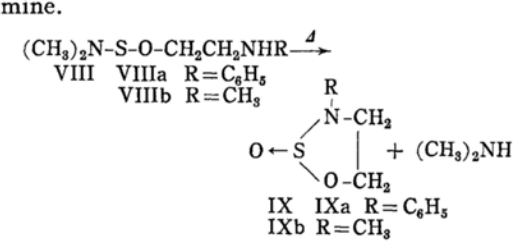
In a similar fashion, when hydrazobenzene was treated with II in benzene at room temperature, azobenzene was obtained in a 78 % yield along with III.



$$II + C_6H_5NHNHC_6H_5 \longrightarrow III + \left[(CH_3)_2N\underset{O}{\underset{\downarrow}{S}}-\overset{C_6H_5}{\overset{|}{N}}-NHC_6H_5\right] \longrightarrow C_6H_5-N=N-C_6H_5 + [(CH_3)_2NSOH]$$

In the case of the reaction of II with α-hydroxycarboxylic esters such as ethyl lactate and ethyl mandelate, however, the thermal decomposition of the corresponsing esters of dimethylamidosulfurous acid obtained as undistillable oily substance did not afford the expected products, α-ketocarboxylic esters, but a large amount of dark colored tarry product and a small amount of unpleasant smelling, low-boiling substances resulted.

Finally, the reaction of II with aminoalcohol was examined. When *N*-phenylethanolamine was added to II in dry ether, III was obtained in a quantitative yield and, after removal of the solvent under reduced pressure, a viscous oily substance remained. The structure of the oily substance was assigned to be β-anilinoethyl dimethylamidosulfite (VIIIa) by its infrared spectrum which has characteristic bands of nitrogen-hydrogen linkage (3200 cm^{-1}) and of ester of amidosulfurous acid (1180 and 900 cm^{-1}). When IXa was heated at 120—130 ℃ for 10 min, evolution of dimethylamine was observed and vacuum distillation of the residue gave cyclic ester of amidosulfurous acid, 3-phenyl-1,2,3-oxathizolidine-2-oxide(IXa), in an 81 % yield. In a similar way, 3-methyl-1,2,3-oxathiazolidine-2-oxide(IXb) was prepared by the reaction of II with *N*-methylethanolamine.



$(CH_3)_2N-S-O-CH_2CH_2NHR \xrightarrow{\Delta}$

VIII VIIIa $R=C_6H_5$

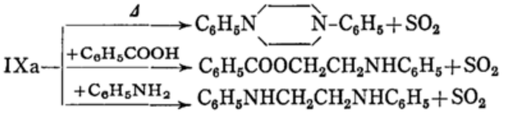
VIIIb $R=CH_3$

$+ (CH_3)_2NH$

IX IXa $R=C_6H_5$

IXb $R=CH_3$

These cyclic compounds were unstable to prolonged heating. For example, when IXa was refluxed in dry xylene for 5 hr, evolution of sulfur dioxide was observed and a large amount of dark colored tarry material was deposited in the flask. From the hot xylene layer, a small amount (6 %) of *N,N'*-diphenylpiperazine was obtained. Further, it was found that when IXa was refluxed in xylene in the presence of benzoic acid or aniline, β-anilinoethyl benzoate or *N,N'*-diphenylethylenediamine was obtained in a 54% or 33% yield, respectively.



Experimental

All melting points and boiling points are uncorrected.

Reaction of *N,N,N,'N'*-Tetramethylsulfurous Diamid-Phenyl Isocyanate Adduct (II) with Benzhydrol. To an ice-cooled solution of *N,N,N,' N'*-tetramethylsulfurous diamide (I) (1.36 g, 10 mmol) in 5 m*l* of dry ether, a solution of phenyl isocyanate (1.19 g, 10 mmol) in 10 m*l* of dry ether was added dropwise with stirring. The mixture was kept standing at room temperature for an hour, and then a solution of benzhydrol (1.84 g, 10 mmol) in ether was added. An exothermic reaction took place and *N,N*-dimethyl-*N'*-phenylurea (III) was precipitated soon. The III was collected and recrystallized from water: yield 1.6 g, mp 134 °C. The filtrate was evaporated at room temperature under reduced pressure, and a viscous oily substance remained. The infrared spectrum of this colorless oily substance shows characteristic bands attributable to ester of amidosulfurous acid (1150 and 900 cm^{-1}). An attempt to purify the oily substance by vacuum distillation led to the decomposition giving 1.05 g (50 %) of benzhydryldimethylamine (Va), bp 130°C/8 mmHg, which solidified soon. It was recrystallized from aqueous ethanol, mp 70.5—71 °C (lit. mp 68.5—70°C).[4]

Found: C, 85.27; H, 8.05; N, 6.67 %. Calcd for $C_{15}H_{17}N$: C, 85.26; H, 8.11; N, 6.63 %.

Similarly, the reaction of II (10 mmol) with 1,3-diphenylallyl alcohol (2.10 g, 10 mmol) gave the corresponding ester of dimethylamidosulfurous acid (IVc) as an oily substance. Its infrared spectrum shows characteristic bands attributable to ester of amidosulfurous acid (1170 and 960 cm^{-1}). When this oily substance was refluxed in benzene for an hour, evolution of sulfur dioxide was observed. After removal of the solvent, the residual liquid was distilled to give 1.40 g (59 %) of 1-dimethylamino-1,3-diphenyl-2-propene (Vc), bp 120—122 °C/0.1 mmHg.

Found: C, 85.87; H, 8.27; N, 6.12 %. Calcd for $C_{17}H_{19}N$: C, 86.03; H, 8.07; N, 5.90 %.

Picrate, mp 175—177 °C (decomp).

Found: C, 59.46; H, 4.96; N, 11.99 %. Calcd for $C_{23}H_{22}N_4O_7$: C, 59.22; H, 4.75; N, 12.01 %.

The reaction of II (10 mmol) with triphenylcarbinol (2.60 g, 10 mmol) gave 1.44 g (50 %) of dimethyl(triphenylmethyl) amine (Vb), mp 93—95 °C (lit. mp 97°C).[5]

Reaction of II with Benzoin. To a solution of 10 mmol of II in dry benzene, a solution of benzoin (2.12 g, 10 mmol) in dry tetrahydrofuran was added dropwise with stirring. After stirring for half an hour at room temperature, the solvent was removed under reduced pressure. Precipitated urea (III) (quantitative yield) was filtered off and the residual liquid (VI) was dissolved in dry benzene. Then the solution was refluxed for an hour, cooled and concentrated under reduced pressure. After standing the residue overnight, precipitated benzil was collected, washed with a small amount of ethanol and recrystallized from ethanol: yield 1.56 g (74%), mp and mixed mp 95—96°C.

Reaction of VI with Ethanol. Ethanol (5 m*l*) was added to the VI prepared by the procedure described above, and the mixture was refluxed for half an hour, cooled and concentrated under reduced pressure. Precipitated benzoin was collected, washed with a small amount of ethanol and recrystallized from ethanol: yield 1.40 g (70 %), mp and mixed mp 134 °C. The filtrate was distilled to give ethyl dimethylamidosulfite (VII): yield 0.8 g (60 %), bp 65—67°C/18 mmHg[1].

Thermal Decomposition of VI in the Presence of *N,N*-Diethylaniline. A solution of VI (10 mmol) and *N,N*-diethylaniline (1.5 g, 10 mmol) in dry benzene was refluxed for an hour. Then 2 m*l* of ethanol was added and the mixture was refluxed for 15 min, cooled and concentrated under reduced pressure. Precipitated benzoin (1.60 g, 76 %), mp and mixed mp 134 °C, was filtered off and the filtrate was distilled to give VII (0.9 g, 66 %), bp 66—68°C/18 mmHg.[1]

Reaction of II with Hydrazobenzene. To a solution of 10 mmol of II in dry ether, 1.84 g (10 mmol) of hydrazobenzene in dry benzene was added dropwise with stirring at room temperature. Precipitated urea (quantitative yield) was filtered off and the orange-red filtrate was concentrated under reduced pressure. The residual liquid was distilled to give azobenzene (1.42 g, 78 %), bp 145—150°C/12 mmHg, which solidified soon. It was recrystallized from aqueous ethanol, mp and mixid mp 67—68°C.

Reaction of II with *N*-Phenylethamine. To an ice-cooled solution of 10 mmol of II in dry ether, a solution of *N*-phenylethanolamine (1.37 g, 10 mmol) in dry ether was added dropwise with stirring. Precipitated urea (III) (quantitative yield) was filtered off and the filtrate was concentrated under reduced pressure. The infrared spectrum of the oily residue shows characteristic bands attributable to nitrogen-hydrogen linkage (3200 cm^{-1}) and ester of amidosulfurous acid (1180 and 900 cm^{-1}). When this oily substance was heated at 120—130°C for 10 min, evolution of dimethylamine was observed. The residual liquid was distilled to give 3-phenyl-1,2,3-oxathiazolidine-2-oxide (IXa), which solidified

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[4] M.M.Sommelet, *Compt. rend.*, **175**, 1150 (1922).

[5] E. Hemilian and H. Silberstein, *Ber.*, **17**, 746 (1884).

immediately: yield 1.48 g (81 %), bp 144 °C/0.07 mmHg.

Found: C, 53.18; H, 5.36; N, 8.37 %. Calcd for $C_8H_9NO_2S$: C, 52.45; H, 4.95; N, 7.65 %.

In a similar manner, 3-methyl-1,2,3-oxathiazolidine-2-oxide (IXb) was obtained in a 21 % yield by treating II with *N*-methylethanolamine, bp 100—102°C/23 mmHg.

Found: C, 30.15; H, 6.56; N, 11.31 %. Calcd for $C_3H_7NO_2S$: C, 29.74; H, 5.82; N, 11.57 %.

Attempts to prepare 3-unsubstituted. oxathiazolidine or benzoxathiazoline by treating II with ethanolamine or *o*-aminophenol were unsuccessful though the urea was obtained in a quantitative yield.

Thermal Decomposition of IXa. When a solution of IXa (1.83 g, 10 mmol) in dry xylene was refluxed for 5 hr, evolution of sulfur dioxide was observed and a large amount of dark colored tarry product was deposited. The hot xylene layer was decanted and the residue was heated with benzene. The hot benzene layer was decanted and combined with the xylene solution. After removal of the benzene and xylene under reduced pressure, the residue solidified. It was recrystallized from ethanol to give *N,N'*-diphenylpiperazine: yield 0.07 g (6 %), mp 164 °C. (lit. mp 164—165 °C).[6]

When the thermal decomposition of IXa was carried out in the presence of *N*-phenylethanolamine, *N,N'*-diphenylpiperazine was obtained in a 25 % yield.

Reaction of IXa with Benzoic Acid. When a solution of IXa (1.83 g, 10 mmol) and benzoic acid (1.22 g, 10 mmol) in xylene was refluxed for 7 hr, vigorous evolution of sulfur dioxide was observed. After removal of the solvent under reduced pressure, colorless crystalline product was obtained. It was recrystallized from ethanol to give β-anilinoethyl benzoate: yield 1.30 g (54 %), mp 73.5—76 °C (lit. mp 77 °C).[7]

In a similar manner, the reaction of IXa with aniline gave *N,N'*-diphenylethylenediamine. It was recrystallized from aqueous ethanol: yield 0.73 g (33%), mp 65.5—67 °C (lit. mp 65 °C).[8]

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6) G. R. Clemo and W. H. Perkin, Jr., *J. Chem. Soc.*, **121**, 647 (1922).

7) E. Bergs, *Ann.*, **332**, 209 (1904).

8) C. A. Bishoff and O. Nastvogel, *Ber.*, **22**, 1783 (1889).